Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 23-78 are pending in the application, with claims 23, 40, 51, 66, 75 and 77 being the independent claims. Claims 39, 50, 65 and 74 have been amended to more particularly point out and distinctly claim the subject matter Applicants regard as the invention, and/or to make explicit that which was previously implicit in the claims. Support for the amendments can be found throughout the specification, *see e.g.*, paragraphs [0059], [0132] and [0133]. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Election / Restriction

The Examiner required restriction under 35 U.S.C. § 121 to one of the following inventions: (I) claims 23-74, drawn to antibody which specifically binds to the polypeptide of SEQ ID NO:2, antibody which specifically binds to the polypeptide encoded by human cDNA in ATCC Deposit No. 209003 and a method for the production of the antibody; and (II) claims 75-78, drawn to a method for screening a compound that binds to a polypeptide comprising amino acids 2-342 of SEQ ID NO:2 and screening a compound which binds to

a polypeptide encoded by human cDNA in ATCC Deposit No. 209003. (*See* Paper No. 7, ¶2, page 2.)

The Examiner further indicated that during a telephone conversation with Elizabeth Haanes on January 24, 2003, a provisional election was made to prosecute the invention of Group I, represented by claims 23-74. (*See* Paper No. 7, ¶2, page 3.) The Examiner required affirmation of this election by Applicants in the response to the Office Action. (*See id.*)

Applicants reiterate the provisional election, *with traverse*, to prosecute the invention of Group I, represented by claims 23-74. This election is made without prejudice to or disclaimer of the claims disclosed in the other group. Applicants reserve the right to pursue the non-elected claims in related applications.

With respect to the Examiner's division of the claims into two groups and the reasons stated therefor, Applicants respectfully traverse. For example, Groups I and II are related as between an antibody and a method of screening for a compound using the recited antibody.

Even assuming, *arguendo*, that Groups I and II represent distinct or independent inventions, Applicants submit that to search and examine the subject matter of both groups together would not impose a serious burden on the Examiner. A search of the art for the claims of Group I should find art relevant to the claims of Group II. Accordingly, it would be a simple matter for the Examiner to search and examine the claimed antibodies and methods together. The M.P.E.P. § 803 (Eighth Edition, Rev. August, 2001) states that:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, Applicants respectfully request that all claims currently under examination be searched and examined together in the subject application. Applicants retain the right to petition from the restriction requirement under 37 C.F.R. §1.144.

Applicants note that the claims of Group I, drawn to an antibody that binds to a protein whose sequence is shown in SEQ ID NO:2 and/or which is encoded by the cDNA contained in ATCC Deposit Number 209003, and the claims of Group II, drawn to a method of screening for a compound which binds to a protein whose sequence is shown in SEQ ID NO:2 and/or which is encoded by the cDNA contained in ATCC Deposit Number 209003, are related as between a product (Group I) and a process for using the product (Group II). Further, the process claims of Group II depend from and include all the limitations of the product claims of Group I.

In light of the decisions in *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ 2d 1663 (Fed. Cir. 1996), a notice was published in the Official Gazette which set forth new guidelines for the treatment of product and process claims. *See* 1184 OG 86 (March 26, 1996). Specifically, the notice states that

> in the case of an elected product claim, *rejoinder will be permitted when a product claim is found allowable* and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim.

Id. (emphasis added). Accordingly, if the elected claims of Group I *are found allowable*, Applicants respectfully request that claims of Group II be rejoined and examined for patentability based on the reasons discussed above.

Objection to the Specification

The Examiner objected to the specification for use of the heading "BRIEF DESCRIPTION OF THE FIGURES." (*See* Paper No.7, ¶3, page 3.) Solely in an effort to expedite prosecution, Applicants have amended the heading to read "BRIEF DESCRIPTION OF THE DRAWINGS" thereby removing the basis for the Examiner's objection.

The Examiner also objected to the specification because the "Applicant has disclosed that clone 2090004 was deposited but has not indicated the address of where it was deposited." (Paper No.7, ¶4, pages 3-4.) Applicants have amended the specification to include the address of the ATCC in accordance with the Examiner's request.

Further, the Examiner asserted that

> the claims require availability of the clone 209003 indicated as deposited with ATCC. Applicant must provide evidence that clones listed in the instant application will be available . . . . An enabled ATCC deposit would satisfy the requirements of 35 U.S.C. § 112, first paragraph.

(Paper No.7, ¶4, page 4.)

Specifically, the Examiner requests that an affidavit or declaration be submitted, assuring that the deposit has been made under the Budapest Treaty, and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, as required by 37 C.F.R. §1.808. In response, Applicants submit herewith a Statement by Lin J. Hymel, Ph.D., Esq., which provides the required assurances.

The Examiner also indicated that the identifying information set forth in 37 C.F.R. § 809(d) should be added to the specification. (*See* Paper No.7, ¶4, page 5.) Applicants point out to the Examiner that paragraphs [0031] and [0032] of the specification contain: (1)

the accession number for the deposit; (2) the date of the deposit; (3) a description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) the name and address of the depository, in compliance with 37 C.F.R. § 1.809(d).

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 39, 50, 65 and 74 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See* Paper No. 7, ¶5, page 5.)

In particular, it is the Examiner's contention that claims 39, 50, 65 and 74 are indefinite because it is unclear what is the immunogen that is introduced into the animal, as the term "carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules." (Paper No. No. 7, ¶5, page 6.)

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claims 39, 50, 65 and 74 to recite that the immunogen introduced into an animal in order to produce an antibody thereto comprises the EBI-2 polypeptide or a fragment thereof. It is not believed that these amendments narrow the scope of the claims.

The Examiner further contended that claims 50 and 74 were indefinite "because the method steps do not achieve the goal of preparing an antibody fragment as stated in the preamble." (Paper No. 7, ¶5, page 6.) The Examiner suggested that additional method steps be included which disclose the production of the antibody fragments and how they are recovered. (*See* Paper No. 7, ¶5, pages 6-7.) In an effort to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claims 50 and 74 to

make explicit that which was previously implicit in the claims, *i.e.*, that after introducing the immunogen, the antibody is recovered and cleaved to produce the antibody fragment.

Applicants believe that the amendments to the claims made herein obviate or overcome the rejections. Accordingly, based on these remarks, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 101

The Examiner rejected claims 23-74 under 35 U.S.C. § 101 because the invention is allegedly not supported by either a specific and substantial utility or a well established utility. (*See* Paper No. 7, ¶6, page 7.) Specifically, it is the Examiner's position that

> since the nucleic acid encoding EBI-2 receptor or the encoded polypeptide are not supported by either a specific and substantial asserted utility or a well established utility, it follows that antibodies that bind to said receptor and methods of producing said antibody [are] also not supported by either a specific and substantial asserted utility or a well established utility . . . .

(Paper No. 7, ¶6, page 15.) Contrary to the Examiner's position, the claimed invention is supported by a specific and substantial asserted utility.

I. Applicants Have Asserted That the Claimed Invention Is Useful.

The specification clearly asserts several utilities for the claimed invention. For example, the specification discloses that monoclonal antibodies raised against EBI-2 can be useful as therapeutics for heart disease, atherosclerosis and restenosis. (*See* specification, paragraph [0035].) In addition, the specification discloses that EBI-2 polynucleotide probes

or antibodies can be used for the detection of EBI-2 expression in vein endothelial cells. (*See* specification, paragraph [0062].) Moreover, the specification discloses that G-protein coupled receptor antagonists which include antibodies (paragraph [0099]) have been used for the treatment of angina pectoris and myocardial infarction (paragraph [0097]) and that G-protein coupled receptor agonists are useful for the treatment of acute heart failure and hypotension (paragraph [0098]). Thus, it is clearly asserted in the specification that the claimed antibodies can be used for the treatment and/or diagnosis of heart disease, including myocardial infarction and angina.

II. The Specification Discloses At Least One Specific Utility.

Applicants submit that the specification discloses a number of specific uses for EBI-2 G-protein coupled receptor molecules and antibodies directed thereto. The Examiner stated that "neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using the EBI-2 receptor or fragments thereof." (Paper No. 7, ¶6, page 14.) However, the specification states that antagonists of the G-protein coupled receptor can be used to treat, *inter alia*, myocardial infarction. (*See* specification, paragraph [0097].) The specification also states that examples of inhibitors of the EBI-2 G-protein coupled receptor include antibodies, small molecules, and soluble forms of the receptor. (*See* specification, paragraphs [0099] to [0102].) Additionally, the antibodies of the invention can be used for the detection of heart disease.

Applicants note that the Utility Guidelines define "specific utility" as a utility that

> is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. . . . For example, indicating that a compound may be useful in treating unspecified disorders, or

> that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. . . . A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

M.P.E.P. § 2107.01 at 2100-32.

The assertion that the claimed antibodies can be used to treat myocardial infarction or detect heart disease is unambiguously specific to the subject matter claimed. The use of these EBI-2 G-protein coupled receptor antibodies to treat, for example, myocardial infarction is a specific use that is not generally applicable to all G-protein coupled receptors, much less to all proteins. In addition, the specification does not merely disclose that the claimed antibodies possesses diagnostic utility. Rather, the specification specifically asserts which disorders can be treated in view of the biological activity of the claimed invention. Accordingly, Applicants have disclosed at least one utility for the claimed antibodies which is specific not only under current case law, but under current PTO Guidelines as well.

III. At Least One Asserted, Specific Utility Is Substantial.

The Examiner stated that "neither the specification nor the art of record disclose any activities or properties that would constitute 'real world' context of use for the claimed EBI-2 receptor and fragments thereof." (Paper No. 7, ¶6, page 14.) Applicants respectfully disagree.

Applicants emphasize that the specification discloses at least one specific and *substantial* utility for EBI-2 G-protein coupled receptor antibodies. The Utility Guidelines define "substantial utility" as a utility that

> defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

M.P.E.P. § 2107.01 at 2100-32.

The Utility Guidelines indicate that substantial utility is a utility that defines a "real world" use. *See id.* Real-world value of an invention requires that "one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980).

The specification discloses a role for EBI-2 in heart disease conditions. (*See* specification, paragraphs [0035], [0097] and [0098].) In addition, the specification provides support for the use of EBI-2 antibodies as a diagnostic for detecting EBI-2. (*See e.g.*, specification, paragraph [0133].) Indeed, as shown in the Hollopeter *et al.* article discussed below and attached herewith as Exhibit A, differential EBI-2 expression may indicate a perturbation in platelet aggregation, which can lead to myocardial infarction. The detection of heart disease and/or treatment of myocardial infarction have real world value.

Hollopeter *et al.* report the cloning of $P2Y_{12}$, a G-protein coupled receptor which has an amino acid sequence identical to EBI-2 and which binds to ADP to mediate platelet aggregation. Hollopeter *et al.* demonstrate that the EBI-2 receptor of the present invention is primarily expressed in platelets (myeloid lineage) and brain (*see* Fig. 4), and that differential EBI-2 expression may indicate a perturbation in platelet aggregation, which can

lead to myocardial infarction. Thus, the disclosure in Hollopeter *et al.* confirms a specific and substantial utility asserted in the specification for the EBI-2 receptor. Antibodies directed to a useful polypeptide are *per se* useful, *e.g.* for isolating and/or identifying it.

Moreover, the specification discloses that G-protein coupled receptor antagonists, such as the claimed antibodies which bind to the receptor, can be used for the treatment of angina pectoris and myocardial infarction. (*See* specification, paragraphs [0097] and [0099].) Hollopeter *et al.* indicate that the EBI-2 receptor is the target of anti-thrombotic drugs which have been demonstrated to be effective in treating a variety of thrombotic diseases such as stroke, myocardial infarction and peripheral vascular disease. Consistent with this assertion, Wang *et al.*, *Arterioscler. Thromb. Vasc. Biol. 23*:357-362 (2003) (Exhibit B), disclose that a small molecule EBI-2 receptor antagonist blocked ADP-induced platelet aggregation and prevented platelet-mediated thrombosis in a canine coronary thrombosis model and suggest a role for the agent in treating myocardial infarction in humans. The same small molecule agent has also been used in treating angina. *See* Chattaraj, *Curr. Opin. Investig. Drugs 2*:250-255 (2001) (Exhibit C).

The references submitted herewith confirm that antagonists to the EBI-2 receptor, such as the claimed antibodies, can be used as suggested in the specification, *i.e.*, to treat myocardial infarction and/or angina. As such, Applicants have disclosed a "therapeutic method of treating a known or newly discovered disease," *i.e.*, the use of EBI-2 G-protein coupled receptor molecules to produce antibodies, to treat, for example, myocardial infarction or angina, or to detect heart disease. (*See, e.g.*, specification, paragraphs [0097] and [0099].) Since one skilled in the art can use the claimed discovery in a manner which

provides some immediate benefit to the public, Applicants submit that the disclosed utilities are substantial utilities as they provide real world value.

In view of the above, Applicants assert that the presently claimed invention possesses a credible, specific and substantial utility that constitutes a patentable utility under 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph - Enablement

A. Claims 23-74

The Examiner rejected claims 23-74 under 35 U.S.C. § 112, first paragraph. (*See* Paper No. 7, ¶ 7, page 15.) In particular, it is the Examiner's position that "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (*Id.*)

For the reasons discussed above in reply to the rejection under 35 U.S.C. § 101, Applicants assert that the claimed invention complies with the current case law and is supported by a specific, substantial and credible utility as well. The Examiner "should not impose a 35 U.S.C. 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. 101 rejection is proper." M.P.E.P. § 2107.01 at 2100-36. Therefore, since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn.

B. Claims 39, 50, 65 and 74

The Examiner also rejected claims 39, 50, 65 and 74 under 35 U.S.C. § 112, first paragraph, "because the immunogen introduced into an animal to produce an antibody or antibody fragment that binds to the polypeptide of SEQ ID NO:2 is not disclosed." (Paper No. 7, ¶ 7, page 15.) The Examiner further rejected claims 50 and 74 "because the method of preparing an antibody fragment, contains the same steps as those used to produce an intact antibody, but with the outcome the fragment is isolated." (Paper No. 7, ¶ 7, page 16.) Applicants submit that the amendments to claims 39, 50, 65 and 74 have rendered these rejections moot. Accordingly, Applicants request that the rejection of these claims be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph - Written Description

The Examiner rejected claims 39, 50, 65 and 74 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. (*See* Paper No. 7, ¶ 8, page 17.) In particular, it is the Examiner's position that

> [t]he instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed immunogen, which when introduced into an animal would produce the antibody that specifically binds to the polypeptide of SEQ ID NO:2.

(Paper No. 7, ¶ 8, pages 17-18.)

Applicants respectfully disagree with the Examiner. However, solely to advance prosecution, and not in acquiescence to the Examiner's rejection, claims 39, 50, 65 and 74 have been amended to recite that the immunogen introduced into an animal in order to produce an antibody thereto comprises the EBI-2 polypeptide or a fragment thereof. As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections Under 35 U.S.C. § 112, First Paragraph - Deposit Rules

The Examiner rejected claims 51-74 under 35 U.S.C. § 112, first paragraph, for lack of enablement, alleging that there is not a repeatable method set forth in the specification for obtaining ATCC Deposit No. 209003 and it does not appear to be a readily available material. (*See* Paper No. 7, ¶9, page 20.) Specifically, the Examiner requests that evidence be submitted that the deposited material will be available and indicates that an enabled ATCC deposit would satisfy the requirements of 35 U.S.C. § 112, first paragraph. (*See id.*)

In response, Applicants submit herewith a Statement Concerning the Deposited cDNA Clone which provides the required evidence. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 51-74 under 35 U.S.C. § 112, first paragraph.

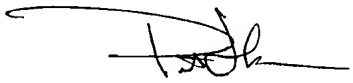
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Peter A. Jackman
Attorney for Applicants
Registration No. 45,986

Date: May 6, 2003

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

Version with Markings to Show Changes Made

In the Specification:

The section after paragraph [0025] was substituted with the following section:

BRIEF DESCRIPTION OF THE DRAWINGS [FIGURES]

The pending paragraph [0033] was substituted with the following paragraph [0033]:

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the mature polypeptide having the deduced amino acid sequence of Figures 3A and 3B (SEQ ID NO:4) or for the mature polypeptide encoded by the cDNA of the clone deposited with the American Type Culture Collection (ATCC),10801 University Boulevard, Manassas, VA 20110-2209, as ATCC Deposit No. 209004 on 4/28/97.

In the Claims:

The following claims 39, 50, 65 and 74 were substituted for the pending claims 39, 50, 65 and 74:

39. (Once amended) A method of producing the antibody of claim 23, comprising:

(a) introducing a polypeptide comprising 30 contiguous amino acids of SEQ ID NO: 2 [an immunogen] into an animal; and

(b) recovering said antibody.

50. (Once amended) A method of producing the antibody fragment of claim 40, comprising:

(a) introducing a polypeptide comprising 30 contiguous amino acids of SEQ ID NO: 2 [an immunogen] into an animal; [and]

(b) recovering an antibody which specifically binds to the polypeptide of SEQ ID NO:2;

(c) cleaving said antibody; and

(d) [(b)]recovering said antibody fragment.

65. (Once amended) A method of producing the antibody of claim 51, comprising:

(a) introducing a polypeptide comprising 30 contiguous amino acids of the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003 [an immunogen] into an animal; and

(b) recovering said antibody [fragment].

74. (Once amended) A method of producing the antibody fragment of claim 66, comprising:

(a) introducing a polypeptide comprising 30 contiguous amino acids of the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003 [an immunogen] into an animal; [and]

(b) recovering an antibody which specifically binds to the polypeptide encoded by the human cDNA in ATCC Deposit No. 209003;

(c) cleaving said antibody; and

(d) [(b)]recovering said antibody fragment.